

REMARKS

Claims 2-4, 7-10, 12-14, 16-27, 29, 30, and 33-36 remain in the application. Claims 2, 4, and 12 have been amended. Claims 12-14, 16-27, 29, 30, 33, and 34 were objected to. Reconsideration of this application, as amended, is respectfully requested.

Claim 2 has been amended to specify that the flowcell has a channel or a chamber formed therein, the channel or the chamber containing the at least one test subject. Support for this amendment can be found at page 9, lines 22-25 and at page 12, line 26 through page 13, line 2 of the specification, and in FIGS. 3, 4D, 4E, and 4F. Claim 4 has been amended to specify that the at least one test material is introduced to the channel or the chamber of the flowcell by means of a liquid. Support for this amendment can be found at page 9, lines 22-25 and at page 11, lines 24-28 of the specification. Claim 12 has been amended to delete the term "for" in line 1 of the claim, between the words "apparatus" and "capable."

Claims 2-4, 7-10, 19, 23, 26, 35, and 36 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement, on the ground that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is respectfully traversed for the following reasons.

Claim 2, as amended, now recites that the apparatus for use in the method has a flowcell having a channel or a chamber formed therein, the channel or the chamber containing the at least one test subject. This feature is supported by the disclosure in the specification. Accordingly, the rejection of claim 2, and the claims depending from claim 2, either directly or indirectly, should be withdrawn. Claim 4, as amended, now recites that in the method of this invention, the at least one test material is introduced to the channel or the chamber of the flowcell by means of a liquid. Accordingly, the rejection of claim 4 should be withdrawn.

Claim 12 has been amended to address the objection noted by the Examiner. Accordingly, the objection to claim 12 and the claims depending from claim 12 should be withdrawn.

In view of the foregoing, it is submitted that claims 2-4, 7-10, 12-14, 16-27, 29, 30, and 33-36, as amended, are in condition for allowance, and official Notice of Allowance is respectfully requested.

The Examiner refused to consider the following references listed in the Information Disclosure Statement mailed June 20, 2000:

Brochure – Oocyte Testing Station (OTC-20) from ALA Scientific Instruments

Brochure – Solution Exchange System (BPS-4/BPS-8) from ALA Scientific Instruments

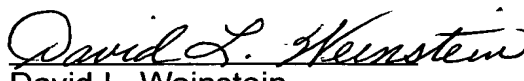
It is believed that these references were not considered on account of the lack of a date. The undersigned was unable to determine the date that these references were available to the public. The undersigned does not believe that these references anticipate the claims of this application or render the claims of this application obvious to one of ordinary skill in the art.

Moreover, the undersigned believes that the foregoing references are cumulative to references that were considered by the Examiner. The Applicants are resubmitting copies of these references for the sole purpose of providing evidence to the public that these references are not being concealed by the Applicants. Applicants will leave the decision to consider these references to the Examiner.

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Respectfully submitted,
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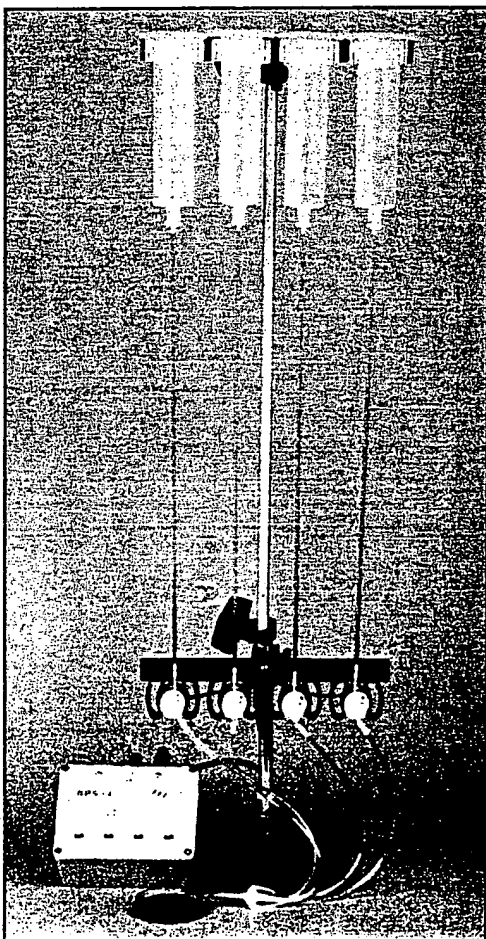
Solution Exchange Systems

for

Cell, Tissue, Oocyte & Bath Perfusion

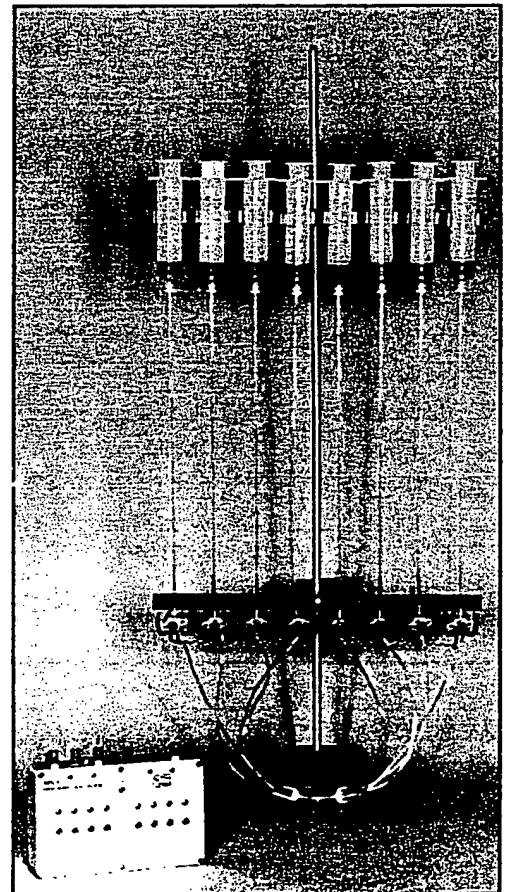
BPS-4/BPS-8

The **BPS-4/BPS-8** are low cost valve controllers for bath, tissue, cell, and Oocyte perfusion. These are gravity feed systems designed to simplify the addition of solutions to the cellular bath. Each channel of the **BPS-4/BPS-8** consists of an electronically controlled pinch valve and a three position toggle switch (1 per valve) for manual control. The **BPS-4** has four BNC TTL inputs that control each valve directly. The **BPS-8** also has four BNC inputs. One serves as an enable and the other three control the valves via a BCD logic pattern. Both of these methods allow for complete control of the valves from commonly used data acquisition systems.



BPS-4 System

Each system consists of a magnetic stand that holds the brackets for the valves and the reservoirs. The standard reservoirs are 60ml luer lock syringes. The standard valves are 2 way pinch valves. There is no need to flush the valve because pinch valves have no internally wetted surfaces. The silicone tubing that is "pinched" is easily replaced or washed out. The entire reservoir assembly as well as individual reservoirs can be moved up/down in order to balance fluid flow. The fluid is directed into the Minimanifold™ and then flows out a single output tube. A pressure system (PR-10 and PR-K), reservoirs of other size, and different valves are available.



BPS-8 System





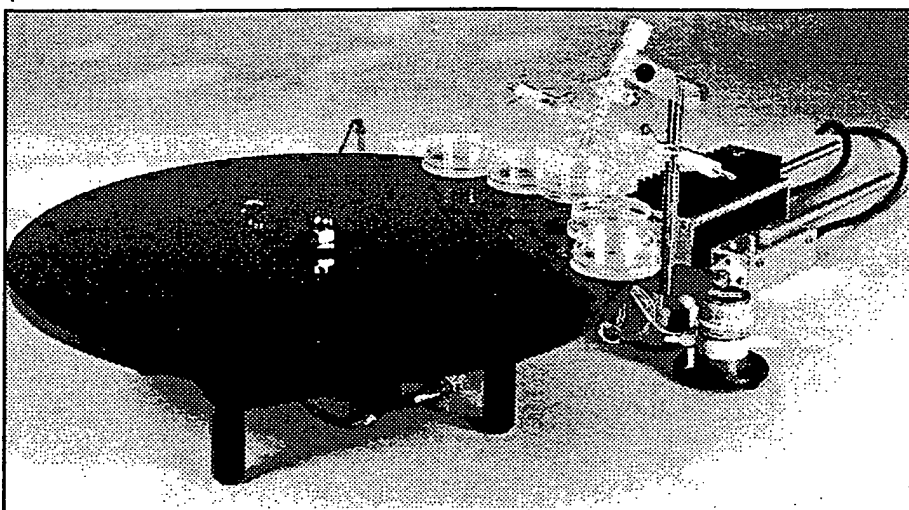
Oocyte Testing Carousel System

OTC-20

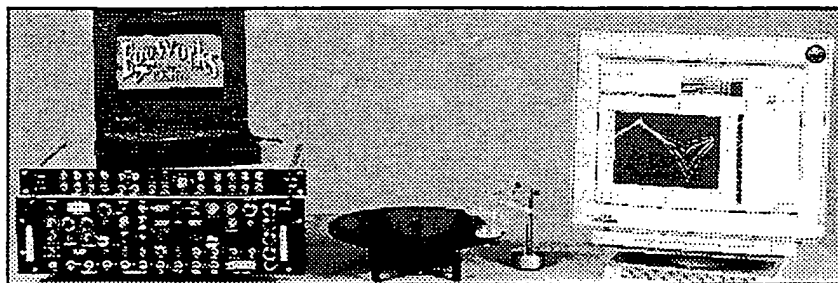
A system for rapid solution exchange
using *Xenopus* Oocytes

The **OTC-20** is a system for rapid solution exchange which is based on the principle of the concentration-clamp technique⁽¹⁾ modified for two-electrode experiments on Oocytes⁽²⁾. It is used to study the kinetics and channel expression of *Xenopus* Oocytes. The **OTC-20** provides mechanical stability, fast solution exchange, and the high quality electronic connections necessary to perform two-electrode voltage-clamp experiments.

The components include a step motor driven turntable with 20 solution positions, control interface, 'Maltese Cross' style Oocyte suspension chamber, and high speed suction valve. The chamber's cross style design allows the Oocyte to be suspended by a simple suction pipette along with two electrodes (held on mechanically stable guideways) which penetrate the egg at 180°. Solution exchange occurs at each station change. A petri dish containing the test solution is lifted into place and a



valve is automatically opened to provide suction for complete solution exchange. Electrical measurements are performed while the Oocyte is completely bathed in the solution. Concentration rise times (τ_{90}) of 10ms have been reported in the literature⁽³⁾. The unique design of the OTC-20 assures that the Oocyte is well protected and never exposed to air during the entire process. The OTC-20 is controlled via TTL from any data acquisition system. Each pulse moves the carousel one position. The direction and speed of the carousel as well as the timing of the solution exchange solenoid valve are user controlled parameters.



When the **OTC-20** is used with **Eggworks** software and a **Turbo TEC Two Electrode Voltage Clamp Amplifier**, complex experiments can be performed.

1) Akaike, N., et al (1986) 'Concentration clamp' study of γ -aminobutyric acid-induced chloride current kinetics in frog sensory neurones, *J. Physiol.*, 379:171-185.

2) Madeja, M., et al (1991) A concentration-clamp system allowing two-electrode voltage-clamp investigations in oocytes of *Xenopus laevis*, *J. Neuro. Meth.*, 38:267-269.

3) Madeja, M., et al (1995) Improvement and testing....., *J. Neuro. Meth.*, 63:211-213.

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